titis B vaccine has made this goal possible. Recent studies have shown that administering HBIG and the hepatitis B vaccine to infants born to HBeAg-positive carrier mothers was 85% to 93% effective in preventing HBV infection in these newborn infants.[13-16] The application of such treatment modalities in HBV-endemic areas will significantly reduce the incidence of the carrier state, chronic hepatitis, and primary hepatocellular carcinoma in these populations.

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Severe Hypermagnesemia Due to Multiple-Dose Cathartic Therapy

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DESPITE DEBATE over their efficacy, magnesium-containing cathartics are widely used in the care of poisoned and overdosed patients.[1] Until recently, such patients generally received only a single dose of cathartic early in the course of their management. There have been no reported cases of hypermagnesemia in patients with normal renal function after single-dose cathartic treatment. As a result, Mg-containing cathartics have been considered safe to use.

In conjunction with multiple-dose activated charcoal therapy, the use of multiple doses of cathartics is now common. Safe dosing limits for Mg have not been investigated for this regimen. We report a case of life-threatening hypermagnesemia in a patient with normal renal function who received excessive Mg during treatment with multiple-dose cathartics.

ABBREVIATIONS USED IN TEXT
GFR = glomerular filtration rate
ICU = intensive care unit

Report of a Case

The patient, a 56-year-old woman, presented to the emergency department three to four hours after an overdose of several drugs taken in a suicide attempt. At her home, medications unaccounted for included as many as 50 Tylenol #3 (acetaminophen, 300 mg; codeine, 30 mg), 21 Placidyl (ethchlorvynol, unknown mg), 34 Fiorinal (butalbital, 50 mg; aspirin, 325 mg; caffeine, 40 mg), and 84 Atarax (hydroxyzine hydrochloride, 25 mg). Other medications were available but accounted for.

The patient was initially awake, alert, but disoriented. Her speech was garbled and inappropriate. Her vital signs were as follows: pulse 92 per minute, blood pressure 140/78 mm of mercury, respirations 18 per minute, and temperature 37.1°C (98.7°F). The remainder of the physical examination elicited no abnormalities. A complete blood count and values for serum potassium (3.9 mEq per liter), blood urea nitrogen (6 mg per dl), creatinine (0.4 mg per dl), glucose (106 mg per dl), and calcium (8.8 mg per dl) were normal. Qualitative urine toxicology screening was positive for butalbital, phenobarbital, salicylate, ethchlorvynol, acetaminophen, benzodiazepine metabolites, phenylethylamine, codeine, and a diphenhydramine-like substance. Quantitative blood levels were as follows: butalbital 31 μg per ml, phenobarbital 7.9 μg per ml, salicylate < 1.5 mg per dl, ethchlorvynol 6.8 μg per ml, acetaminophen < 2 μg per ml, and benzodiazepine < 0.5 μg per ml. Quantitative levels for the other agents found in the urine were not available.

There was no change after administering 0.8 mg of naloxone hydrochloride intravenously. Gastric lavage recovered pill fragments. She was given 100 grams of activated charcoal and 15 grams magnesium sulfate and admitted to the intensive care unit (ICU).

In the ICU, persistent confusion and agitation were noted. Pupils were dilated but reactive. Vital sign examination showed her pulse to be 98 to 110 per minute, blood pressure 110 to 170/70 to 94 mm of mercury, and respirations 16 to 22 per minute. Treatment initially consisted of intravenous hydration, supplemental oxygen, and 50 grams of activated charcoal in water every two hours. After five hours (nine hours after ingestion), a regimen of 75 grams $MgSO_4$ (150 ml of a 50% solution of $MgSO_4$) given every hour was begun unintentionally. A large diarrheal stool was noted two hours later. Four hours after starting the regimen of $MgSO_4$, lethargy was noted but deep tendon reflexes were present and the patient responded to commands. Two hours later, after the patient had received six doses of $MgSO_4$ (a total of 465 grams

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since admission), a cardiorespiratory arrest occurred. At the time of the arrest, bradycardia, coma, apnea, and no palpable blood pressure were noted. Resuscitative efforts included endotracheal intubation and intravenous administration of atropine sulfate and epinephrine. The subsequent course is shown in Figure 1. One and a half hours after the arrest, her serum Mg level was 21.3 mEq per liter (normal 1.5 to 2.5) and calcium was 9.9 mg per dl (normal 8.5 to 10.5). After resuscitation, blood urea nitrogen and creatinine levels were 4 and 0.6 mg per dl, respectively.

Profound hypotension was treated with fluid boluses and the administration of dopamine hydrochloride and norepinephrine bitartrate. During the first six hours following the arrest, 308 mEq of sodium bicarbonate was given. Furosemide, 40 mg, was given intravenously because of a possible fluid overload. Pronounced hypokalemia (1.6 mEq per liter) was noted and treated with potassium replacement. Hyperglycemia ensued (540 mg per dl), and insulin was given. Her urine output was less than 30 ml per hour for the first three hours after her arrest but then gradually increased to 200 to 300 ml per hour seven hours after the arrest. Blood urea nitrogen and creatinine measurements every two to four hours following the arrest remained normal, with maximums of 10 and 0.6 mg per dl, respectively.

Her serum magnesium levels gradually returned to normal with supportive care only (see Figure 1). The patient showed withdrawal to pain 10½ hours after the arrest, followed simple commands 14 hours after the arrest, and the endotracheal tube was removed 31 hours after the arrest.

She remained confused, and hypertension developed, requiring treatment. Her subsequent course was otherwise uneventful, and she recovered completely.

Discussion

In the absence of renal dysfunction, symptomatic hypermagnesemia is unusual, but has occurred after rectal dosing and after combined oral and rectal dosing in patients with bowel obstruction, megacolon, or bowel perforation.[2,3] In patients with renal failure, symptomatic hypermagnesemia has occurred after the use of Mg-containing antacids, cathartics, enemas, parenteral infusions, dialysate, and Renacidin.*[2,3] Until recently,[4] hypermagnesemia after oral Mg administration had not been reported in patients with normal gastrointestinal tracts and renal function. Surprisingly, other than intentional hypermagnesemia for the treatment of eclampsia or preeclampsia, symptomatic hypermagnesemia due to parenteral Mg dosing is infrequent.[2,3]

There have been no reports of Mg toxicity after single-dose cathartic therapy, suggesting that standard doses (see Table 1)[5] are safe when given once. While the use of multiple doses of Mg-containing cathartics is clearly increasing, safe dosing strategies have not been studied.

Magnesium Homeostasis

Normally, 30% to 40% of total dietary Mg—average, 25 mEq per day[6,7]—is absorbed with more (up to 76%) or less (as low as 24%) being absorbed during low and high Mg intake, respectively.[6,8] The fractional absorption of Mg after oral cathartic administration is unknown; 30 grams of $MgSO_4$ contain 2.9 grams (240 mEq) of Mg (see Table 1). Any significant absorption of this amount clearly would require an increase from the baseline renal Mg excretion to maintain a normal Mg concentration. The patient in the present case received 465 grams of $MgSO_4$ (44.6 grams, 3,720 mEq of Mg) over ten hours. About 97% of the dose was given in the last five hours of this period. In the report by Fassler and co-workers of cathartic-induced hypermagnesemia without renal impairment, 90 grams (7,380 mEq) of Mg was given, evenly distributed over an 11-hour period, yielding a Mg level of 13.2 mEq per liter.[4]

Normally, renal Mg excretion amounts to only 100 to 150 mg (8 to 12 mEq) or roughly 3% of the total filtered Mg per day.[7] When hypermagnesemia occurs, renal tubular reabsorption declines, and as much as 97% of filtered Mg is excreted.[7] The maximum Mg load that can be excreted without Mg accumulation and a resultant hypermagnesemia is not known. In patients given 5.6 grams (467 mEq) of Mg per day by mouth, renal excretion increased to 500 to 600 mg (42 to 50 mEq) per day, and normal Mg concentration was maintained; presumably, decreased gastrointestinal fractional absorption limited the absorbed Mg dose to help maintain homeostasis.[6] Six grams (500 mEq) per day has been suggested as an achievable maximum daily Mg excretion.[4] These data are derived from a hypermagnesemic dog model,[9] and its relevance to humans is unknown. One patient with a serum Mg level of 17.3 mEq per liter excreted 196 mg (16.3 mEq) in three hours,[10] but no other data on maximal human excretion capability are available. The degree of renal impairment affects excretion capability. While patients with creatinine clearance values of 30 ml per minute or less are at the greatest risk for the development of hypermagnesemia,[2] life-threatening hypermagnesemia has recently been reported with only minimal renal dysfunction after multiple-dose cathartic therapy in standard doses.[11] In the present case, administering high doses of hypertonic $MgSO_4$ may have led to a significant loss of extracellular fluid into the gastrointestinal tract. Stool losses were not accurately quantified. With or without such intravascular volume loss, decreasing blood pressure due to developing hypermagnesemia probably led to a decreasing glomerular filtration rate (GFR). Such a decrease in the GFR would rapidly result in further Mg accumulation. Although this was almost certainly the case, it remains speculative because there were no hourly urine output determinations before the patient's cardiorespiratory arrest.

Magnesium Toxicity

The signs and symptoms seen in this case were consistent with those seen in cases of severe hypermagnesemia (see Table 2), although the course may have been altered by the apparent anticholinergic overdose (hydroxyzine). Findings were initially attributed to the patient's overdose, and hypermagnesemia was not considered. Deep tendon reflexes disappear at Mg levels of 7 to 10 mEq per liter, respiratory depression and unresponsiveness occur above 9 to 10 mEq per liter, and cardiac arrest is generally seen at levels above 14 to 15 mEq per liter.[2] Two and a half hours before the arrest, the deep tendon reflexes were present and the patient was responsive, suggesting that the subsequent rise in the serum Mg level was rapid. Whether severe hypermagnesemia causes actual coma is unclear. Unless hypermagnesemia is protracted or there is a defect in the blood-brain barrier, the central nervous system is generally not greatly depressed. Unless hypotension, hypoxia, or other metabolic causes of coma are present, the unresponsiveness of patients with severe hypermagne-

*A product used in urolithiasis. Active ingredients: citric acid, anhydrous, and D-gluconic acid (Guardian Chemical, Smithtown, NY).

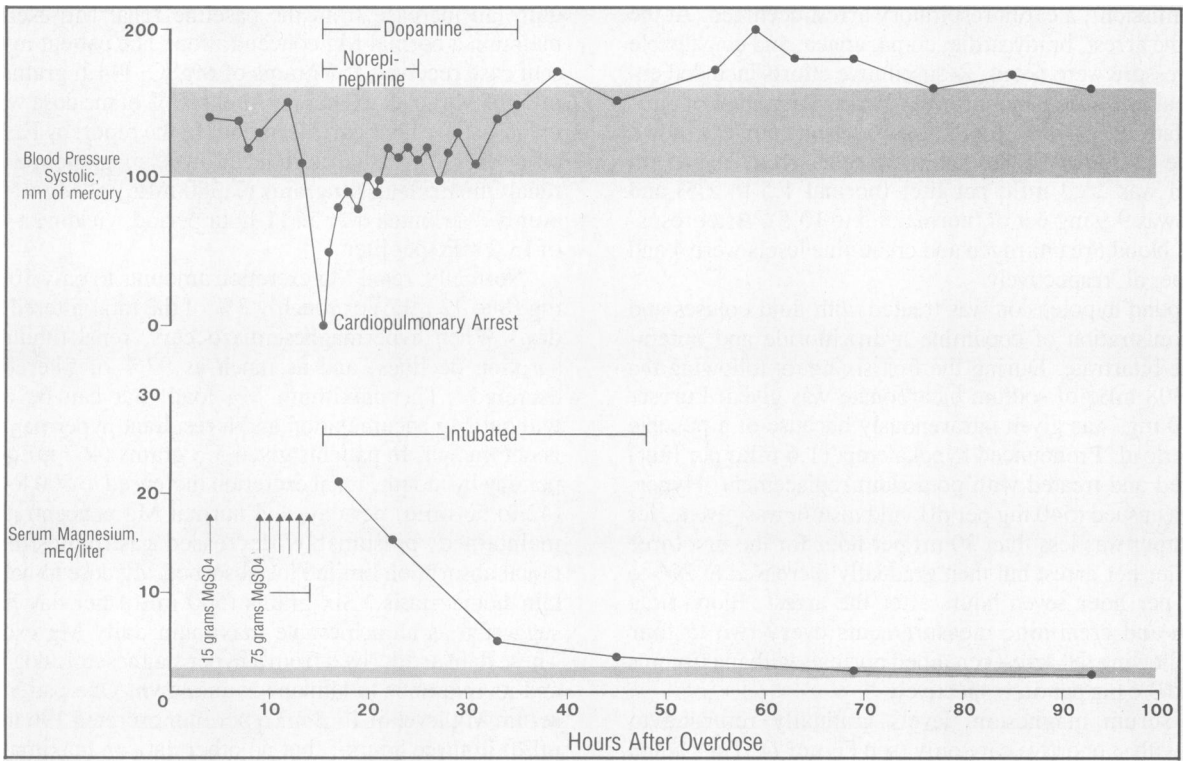

Figure 1.—The graph shows the clinical course and serum magnesium levels in a patient with severe hypermagnesemia due to multiple-dose cathartic therapy. The shaded areas indicate normal ranges.

semia is often due to complete neuromuscular paralysis.[2] Actual central nervous system depression certainly may have occurred in this case due to brain injury from cardiac arrest and hypotension.

The hyperglycemia and hypokalemia were probably not directly due to hypermagnesemia. Although hypermagnesemia inhibits the release and action of endogenous catecholamines,[2] some degree of hyperglycemia would be likely after the high dose of exogenous catecholamines used in this patient's resuscitation and supportive care. Whether or not the resultant hyperglycemia was exacerbated by unsuspected glucose intolerance was unknown at the time of discharge. Although early work suggested that hypermagnesemia might cause hypokalemia, this has not been substantiated.[2] The likely sites of potassium loss in this patient included cathartic-induced diarrhea and urinary losses due to glycosuria, furosemide therapy, and hypotension-induced renal sodium conservation. Certainly sustained hyperglycemia, insulin therapy, and the aggressive use of bicarbonate contributed to hypokalemia by producing intracellular potassium shifts.

The patient's clinical recovery corresponded to the fall in Mg levels (see Figure 1). Once Mg dosing was discontinued and the blood pressure and GFR were adequate to allow renal Mg elimination, levels declined rapidly.

Treatment of severe hypermagnesemia includes discontinuing Mg intake, maintaining normal urine output or hemodialysis if renal impairment is present, supportive measures to correct hypoventilation and hypotension, and administering calcium.[2,3,6] There is no doubt that severe hypermagnesemia should be treated with dialysis in patients with compromised renal function.[2-4,6] As this case shows, however, when renal function and the GFR are adequate, even life-threatening hypermagnesemia can be treated without dialysis.[4] Calcium has been shown to reverse both Mg-induced hypotension and paralysis.[2] Although sustained hypermagnesemia can cause hypocalcemia,[2] calcium levels were normal in this case. Calcium directly antagonizes the effects of hypermagnesemia and is indicated even in patients with normal calcium levels when serious Mg toxicity is present. Calcium was not used in the present case because the diagnosis of hypermagnesemia was not made initially.

TABLE 1.—*Magnesium Content of Standard Cathartic Doses**

Cathartic	Magnesium Content	
	Milliequivalent	Milligram
Magnesium sulfate solution ($MgSO_4 \times 7\ H_2O$)/gram	8	96
Adult dose, 30 grams	240	2,880
Pediatric dose, 250 mg/kg	2/kg	24/kg
Magnesium citrate ($C_{12}H_{10}Mg_3O_{14}$)/dl	0.8	9.6
Adult dose, 300 ml	240	2,880
Pediatric dose, 4 ml/kg	3.2/kg	38.4/kg

*From Rumack.[5]

TABLE 2.—*Clinical Findings of Hypermagnesemia**

Serum Magnesium, mEq/liter	Clinical Findings
3- 9	Hypotension, cutaneous flushing, nausea, vomiting
5-10	Electrocardiographic changes, decreased deep tendon reflexes, central nervous system depression (see text), bradycardia
> 9-10	Respiratory depression, unresponsiveness
>14-15	Asystole, cardiac arrest

*From Mordes and Wacker.[2]

Conclusion

This case provides further evidence that orally adminis-

tered Mg-containing medications can cause hypermagnesemia in patients with normal renal function. With the increasing use of multiple doses of Mg-containing cathartic therapy for poisoned or overdosed patients, more patients will receive higher Mg loads. Safe upper limits for Mg dosage by this route have not been established. Therefore, when treating patients in this manner, physicians should consider monitoring Mg levels and renal function and must be vigilant for signs and symptoms of hypermagnesemia. An alternative is the use of sorbitol[1,5] as a cathartic, although its safety in multiple doses has not been well studied.

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Occult Mineral Oil Pneumonitis in Anorexia Nervosa

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ANOREXIA NERVOSA-BULIMIA is a disorder primarily affecting young, white, middle-class women.[1-3] Due to the altered nutritional state associated with this condition, many secondary medical disorders occur.[4] Associated pulmonary complications are uncommon.[1,2] We present the case of a patient with a previously unreported complication of anorexia nervosa—occult mineral oil aspiration leading to respiratory failure.

Report of a Case

The patient, a 36-year-old woman, had a 20-year history of anorexia nervosa and bulimia associated with diuretic, laxative, and alcohol abuse plus depression with multiple suicide attempts. She was admitted due to the recent development of peripheral edema with a 12-kg (25-lb) weight gain. On physical examination on admission she was unkempt, cachectic, and appeared chronically ill, with ascites and anasarca, but in no acute distress. The cardiopulmonary examination showed no abnormalities. Laboratory evaluation revealed a hematocrit of 33% and abnormal liver function test values, including an albumin of 1.4 mg per dl. The leukocyte count, electrolytes, renal function, chest x-ray film, and an electrocardiogram (ECG) were normal.

Enteral alimentation and vitamin replacement were initiated, with a 3-kg (6-lb) weight gain over the next week. On the seventh hospital day, acute respiratory distress developed, and the patient had a temperature of 38.6°C (101.4°F). She said her only new symptom was dyspnea. On physical examination there were bilateral rales, expiratory wheezes, bibasilar dullness, jugular venous distension with a summation gallop, and anasarca. Laboratory tests showed a hematocrit of 26%, a leukocyte count of 19,600 per μl and arterial blood gas values with the patient breathing 100% oxygen by mask of pH 7.37, a partial carbon dioxide pressure of 44 torr, and a partial oxygen pressure of 62 torr. The ECG was unchanged. A chest x-ray film (Figure 1) showed an increased cardiac size, hilar haziness, bilateral alveolar infiltrates predominantly in the upper lobes, and bilateral pleural effusions. A bilateral thoracentesis revealed transudates, and a sputum Gram's stain showed mixed flora. Vigorous treatment including diuresis, transfusion, bronchodilators, and antibiotic coverage for nosocomial aspiration was initiated.

Despite the above treatment, the patient's condition deteriorated, requiring intubation and mechanical ventilation. Oxygen concentrations in the 70% to 80% range with 10 cm water of positive end-expiratory pressure were initially necessary to maintain adequate oxygenation. A right heart catheterization showed a cardiac output of 6.3 liters per minute and a mean pulmonary artery wedge pressure of 26 mm of mercury. On a gated blood pool study, there was a reduced left ventricular ejection fraction of 52% with no regional wall abnormalities, and an echocardiogram revealed septal dyskinesis, mild generalized hypokinesis, and a small pericardial effusion. Several sputum cultures grew mixed flora.

Five days after intubation, a temperature of 38.5°C (101.3°F) developed, and chest x-ray film findings worsened. A fiberoptic bronchoscopy showed no abnormalities. Trans-

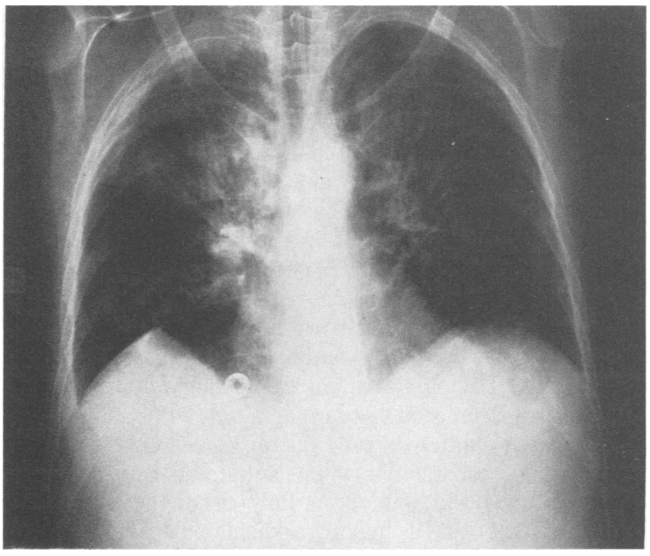

Figure 1.—A chest roentgenogram shows acute respiratory failure with upper lobe pneumonitis and superimposed congestive heart failure.

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